AMERICAN JOURNAL OF PHARMACY

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EDITORIAL

On these pages the editor offers his opinions, unshackled by advertising patrons and unrestrained by anything save a sense of the decent and the truthful—the editor, alone, is responsible for their type, their tone and their tenor.

WORTHY OF SUPPORT

EDUCATION in pharmacy has considerably advanced in the course of the past decade. In all colleges under the jurisdiction of the Council on Education of the Association of Colleges of Pharmacy there is operating a four-year balanced course leading to the degree of Bachelor of Science in Pharmacy, hence rendering this degree a pre-requisite to State Board registration.

Some charge that the practice of pharmacy is so reduced in its opportunity to render professional service that this long training is superfluous, and that the average graduate scarcely has a chance to use it.

This is not so!

Educators in the field know that there are more opportunities today for well trained pharmacists than have ever before been available. They know this clinically.

They also know *that there is no four-year course in any other field that so comprehensively educates its pupils, fitting them, and fitting them well, not just for their special field but also for any of the diversifield fields in the sciences supporting public health,* and this is especially true if there has gone along with collegiate training an experience in the retail pharmacy. Even though the modern tinselled pharmacy seems hardly a fit place for young people with professional ideals to gain useful experience, it does afford a certain training in human relations, and it does, when at its best, instill some very useful practicalities as well as ethics and esthetics into young people's performances.

Unfortunately, too many persons judge and misjudge pharmacy on the sandwich basis, a premise quite as unsound as judging medicine darkly through the chiropractic glass.

Pharmacy as practiced today is a better pharmacy than ever it has been practiced before. It is more serviceable, safer, truer to its mark. Thanks to diversified agencies, particularly the large drug

houses, with their control and research departments, the manufacture of medicines is more responsibly done.

And in such manufacture, as well as in the retail pharmacy and in the hospital pharmacy are ample opportunities for well-trained young men and women.

Thorough education *is* necessary and well organized and well supported colleges are necessary to do this.

No college of pharmacy is self-supporting. Indeed every institution under the Council's ægis must find each year, considerably more money than is received from students' fees.

From certain individuals and firms, whose well-earned fortunes were made in and from the pharmaceutical field, have come splendid gifts, a token of recognition of their indebtedness to these fountain-heads of pharmacy—the colleges; and proving the good in their hearts.

I should like to have the privilege of naming them here, but it would not be in good taste.

Other individuals and firms whose fortunes have been similarly made, prefer to divert their donations elsewhere, and far afield from the source of their fortune.

I should like to have the right to name them here, but neither would that be in good taste.

Anyhow, most pharmacists know all about it!!

IVOR GRIFFITH.

ORIGINAL ARTICLES

CHEMICAL MICROSCOPY OF FATS AND WAXES
V. CHAULMOOGRA OIL

By L. Wilson Greene
Aberdeen, Maryland

IN a previous number of this JOURNAL, the author described several microchemical reactions which might prove of value for identifying castor oil (1). The present communication deals with another fat of pharmaceutical interest, chaulmoogra oil. While only two specimens of this fat have been examined certain consistent results have been obtained, and it is believed that the methods here described will be useful for identification purposes. No references to previous work on the microchemical identification of chaulmoogra oil have been found.

EXPERIMENTAL

Specimens Used

Specimen No. 45. Obtained from the Oil, Fat and Wax Laboratory, Bureau of Chemistry and Soils, U. S. Department of Agriculture, in 1933. Experimental work was conducted in 1933, 1934 and 1938.

Specimen No. 291. (From *Taraktogenos Kurzii*). Obtained from the Department of Chemistry, University of Hawaii, in 1934. Experimental work conducted in 1937 and 1938.

Normal Appearance

Each specimen contained a considerable quantity of separated "stearin" (room temperature 24°). The sample was shaken to disperse the solid matter uniformly through it and a drop was transferred to a microscope slide, using a small glass rod. The drop was covered with a cover slip and examined under the microscope at a magnification of 100X. Anisotropic crystals (Fig. 1) were observed in polarized light.

The preparations made above were warmed to melt the crystals and then set aside at 4 degrees for one-half hour. They were examined again and were found to contain the same type of crystals, only the forms were larger and more scattered.

Reactions With Alcoholic Alkalies

The general method for preparing these saponifying reagents was described in the communication on castor oil (1) and need not be repeated here. The samples were warmed to melt the "stearin" and mixed thoroughly before withdrawing the test drop.

A drop of the specimen, about 2 mm. in diameter, and an equal amount of reagent were intimately mixed on a slide with the aid of a glass rod. The preparation was then covered. In every instance an amorphous isotropic soap was formed at first and then crystals appeared dispersed through the mass. The following results were obtained:

Reagent used	Average time for appearance of crystals, min.	Crystal form
NaOH in ethyl alcohol	40	Fig. 2
KOH in ethyle alcohol	15	Fig. 3
NaOH in *n*-butyl alcohol	70	Fig. 2
KOH in ethyl alcohol	15	Fig. 3

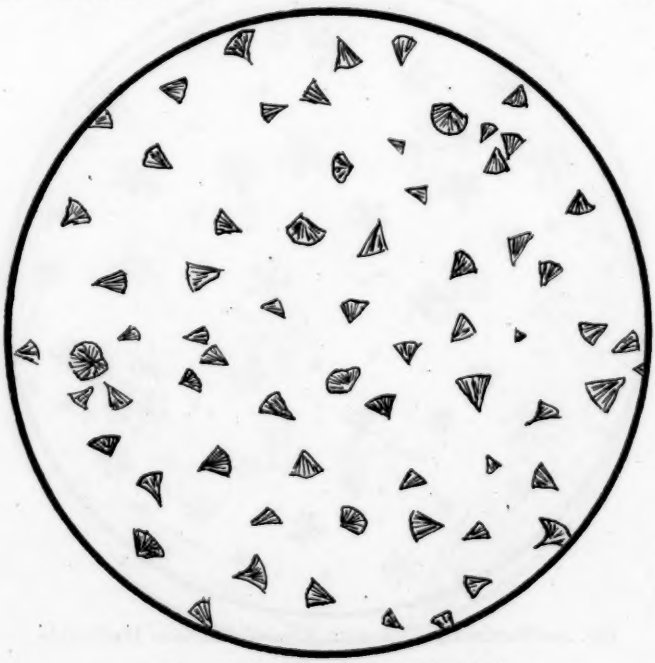

Fig. 1—Chaulmoogra Oil "Stearin"

All crystalline reaction products were anisotropic and were observed at 100x magnification. Most of the crystals were practically invisible in ordinary transmitted light but were clearly resolved when the light was polarized.

Reaction With Phenylhydrazine

Two different lots of reagent were used. One of these was an Eastman Kodak Company product melting at 19-19.5 degrees, and the other was from the Coleman & Bell Company; the latter product having a melting point of 18-19 degrees.

A 2-mm. drop of the specimen (previously warmed) and an equal amount of phenylhydrazine were mixed together on a slide by stirring with a glass rod. The preparation was covered with a slip and then heated carefully over a flame until white fumes were evolved from under the slip. After allowing the slide to cool, periodical examination at 100x showed that branching crystalline forms began to appear in about one-half hour and after twelve hours the entire

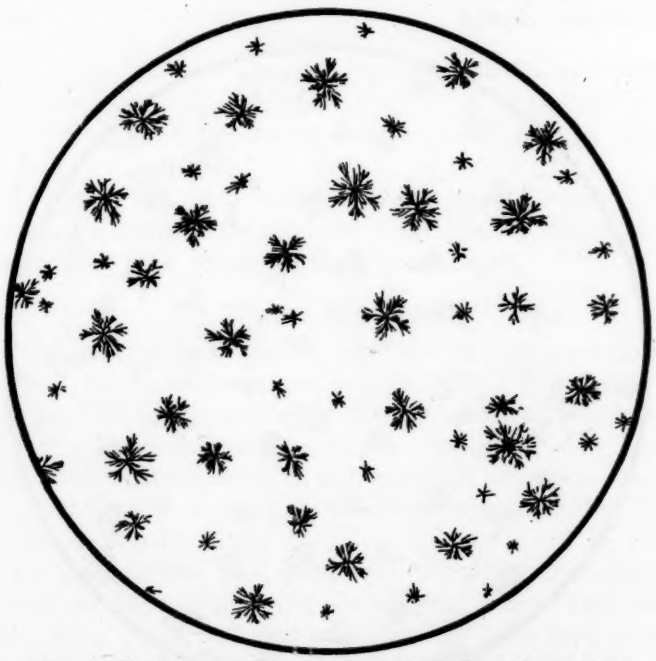

Fig. 2—Chaulmoogra Oil with Alcoholic Sodium Hydroxide

preparation was filled with crystals as illustrated in Fig. 4. These were anisotropic.

No difference could be detected in the results obtained with the two lots of reagent.

Discussion

The reaction products with alcoholic alkalies are not particularly characteristic of chaulmoogra oil because somewhat similar forms have been obtained with other fats. These reactions, used in conjunction with that given by phenylhydrazine, should be useful in establishing the identity of chaulmoogra oil.

The possibility of using phenylhydrazine as a microchemical reagent for fats was indicated by the author about five years ago (2). It was recognized then that its main disadvantage was the length of time required for crystals to form when it was heated with various fats. In some instances almost two weeks elapsed before crystals appeared. Mehlenbacher (3) tried this reagent but the results did not meet his expectations and further work by the author, using about 80 fats, has shown that its application is definitely limited.

Fig. 3—Chaulmoogra Oil with Alcoholic Potassium Hydroxide

With the two specimens of chaulmoogra oil, however, phenylhydrazine readily and consistently gave a crystalline reaction product which appears to be characteristic, although hydnocarpus oil (from *Hydnocarpus Wightiana*) produces crystals which could be confused with those obtained with the former. The crystals given by hydnocarpus oil and alcoholic alkalies are different from those formed with chaulmoogra oil, being of a more branching habit.

Fig. 4—Chaulmoogra Oil with Phenylhydrazine

Acknowledgment

The author wishes to thank Dr. G. S. Jamieson, of the U. S. Department of Agriculture, and Professor J. H. Payne, of the University of Hawaii, for the specimens of chaulmoogra oil used in this work. The latter also furnished the hydnocarpus oil.

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PLAIN TALK ABOUT ADIPOSE TISSUE

By T. Swann Harding

THE obesity problem is very simple. You merely reach middle age and your body starts to lay down deposits of adipose tissue. Adipose tissue consists chiefly of triolein ($C_3H_5(OOC.C_{17}H_{33})_3$), tripalmitin ($C_3H_5(OOC.C_{15}H_{31})_3$), and tristearin ($C_3H_5(OOC.C_{17}H_{35})_3$). Adipose tissue makes you fat. It is as simple as that.

About three-quarters of the deposit is composed of what we may call olein, for short—a soft fat which melts easily and can be derived from both animal and vegetable foods. People who fatten themselves on sugar and starchy foods possess a harder, firmer fat and do not appear so flabby as those who fattened up on oily dishes.

Primarily the adipose tissue is derived from the food that we eat. Man was intended to counter appetite with exercise, but the older he gets the less likely he is to do so. Appetite ceases to be an accurate guide to his energy requirements and his weight-regulating mchanism goes haywire. In other words he no longer dissipates slight excesses of food as heat. He stores fat.

This brings us to the famous calorie which is that amount of energy required to raise the temperature of one kilogram (say about a quart) of water from zero to one degree Centigrade. A gram (say about one-thirtieth of an ounce) of fat yields 9.3 calories, a gram of carbohydrate or of protein yields 4.1 calories, a gram of alcohol yields 7 calories. Remember the mixed drinks therefore.

Now the average sedentary young man needs roughly 2800 calories of energy to get through a day. H expends 1700 calories of it just existing; it takes that to run his organism, digest his food, and so on. He requires an additional 500 calories to be up and about except when sleeping. He uses up about 600 calories in exercise.

If he rises from the chair in which he is sitting, crosses the room, opens the door, closes it, returns to the chair, and sits down he expends 1 calorie. His bodily activities lop off 5 per cent. of the value of his food—muscular movements, glandular activities, masticating, swallowing, digesting, and absorbing food and so on. His brain work requires no calories at all.

A very quiet sedentary worker may get along on 2370 calories a day. He uses 520 of them during his 8-hour sleep. It takes 880 of them to be up and around the house for 8 hours at 110 calories per hour and 770 of them at the same rate to cover 7 hours work. In his one-hour walk to and from the office he expends 200 calories.

A man at physical work will expend from 1500 to 2000 calories daily on that work, depending upon how much he does and upon his skill, for skill leads to economy of effort. It takes 57 calories per mile to walk. A round of golf or a three-set single at tennis will expend about 300 calories. So much for the out-go.

Now let us view this in terms of the in-take. It is somewhat distressing for the obese to reflect that 1 lump of sugar supplies sufficient calories for a 100-yard run; 3 lumps will sustain a 1-mile walk; 15 lumps would require a set of tennis to work off. A glass of milk is good for a 3-mile walk, a medium-sized potato (5 ounces) for 9 holes of golf, a pint of beer for 15 holes, and a 2-ounce bar of chocolate for a complete round of golf. It is easy to see how an extra pat of butter taken daily for years may produce a man-mountain.

Mayonnaise dressing rates 120 calories per tablespoonful. While clear soup contains no calories a cup of vegetable soup will run 37 though it contains little fat. A glass of sauterne supplies 87 calories, a glass of champagne (sweet) 180, a glass of sherry about 90, and a jigger of whiskey, brandy, gin, or rum 82 calories. The Bronx cocktail rates 98 calories, the Bacardi 105, the sweet Martini 122, the dry Manhattan 134.

The cause of corpulence seems to dawn upon us here. Fat comes largely from food and drink; the rest deposited in the human body gets there through lack of exercise or glandular deficiency. We may eat too much food or the wrong foods; we may have a faulty basal metabolism which makes the wrong response to foods; or we may be too sedentary.

The poor get fat usually on sugar, bread, pastries and potatoes; the rich add fried foods, animal fats, cream, oils and so on. Both types increase the caloric value of their diets by indulgence in cakes, confections, and alcoholic beverages, adding these to an already adequate diet—speaking from the standpoint of energy content.

Fat comes from an excessive intake of fuel foodstuffs regardless of what other causes may be cited, like faulty metabolism, lack

of due response to temperature or to exercise, and glandular deficiency. The pituitary, the thyroid, the adrenal, and the gonadal glands may all act up so as to enhance the individual's chance of becoming obese. There are also certain obscure irregularities of the fat-storage mechanism in certain people.

But always—*fat comes from food.*

A doctor reporting on 184 cases of adult obesity found that food was the cause of fatness in 106 and food and alcohol in 50 additional cases. Ten cases were caused by sedentary habits due in 8 to occupation and in 2 to physical infirmity. There were only 16 glandular cases and the other 2 were accounted for as after effects of encephalitis lethargica.

In 16 juvenile cases 11 were caused by food and only 5 from glandular disturbance. Hence about 85 per cent. of fat adults and 70 per cent. of fat children become obese because they eat too much.

What are the consequences of obesity? Gastric dyspepsia is the first symptom usually manifested. Other abnormalities follow such as raised blood pressure, albuminuria, glycosuria, gout, rheumatism, heart trouble and so on. The joints, voluntary muscles, cardiovascular system, respiratory system, and alimentary tract all suffer more or less. Glandular obesity produces its own peculiar symptoms.

Obese patients are bad risks. All doctors and surgeons agree on that. Insurance companies know that they tend to die younger than the thin people.

What is the "ideal" weight? Is there such a thing? A man's ideal weight is probably that he had at 25 years of age; a woman's that she had at 20. If the number of inches above 5 feet in height is multiplied by 5½ and this result is added to 110 the "ideal" weight is approximated in pounds.

How can obesity be treated?

The first admonition is: *Avoid all drug treatments for obesity.* These are universally a snare and a delusion. They are, broadly speaking, of three types:

1. Camouflaged purgatives or laxatives; 2. Powerful drugs that speed up metabolism but that are always dangerous for laymen to use and are sometimes hazardous even under medical supervision; 3. Drugs intended to depress appetite. To this list may be added the concentrated foods sold as obesity cures but which are intended to kill appetite before meals.

The average trade-marked obesity "cure" usually carries with it certain information about diet and exercise. This information is often quite accurate and if followed carefully will enable the buyer to reduce weight whether she uses the "cure" or not. Low food intake, additional physical exercise, and frequent hot baths always tend to reduce weight.

Thryoid or dinitrophenol are drugs that often occur in obesity cures. Thyroid should be used only under a physician's direction. It is effective in but a few kinds of obesity. The process is always expensive for frequent basal metabolism tests are needed to check up. Dinitrophenol should never be used by laymen and the more careful physicians think it too hazardous even for them to use.

The first step in weight reduction should be a thorough physical examination by a competent physician. He can determine whether the obesity is glandular in origin and also just how much exercise or fasting the individual can undertake safely.

Exercise must always be used in moderation. An increase in general daily activity and the pursuit of some active pastime may be advised for those no more than 15 pounds overweight whose hearts and circulation are unimpaired. The prescription may be automatic punch balls, dumb-bells, Indian clubs, muscle developers, sculling machines and other methods of inducing rapid muscular movements to burn more calories as in fencing, tennis, gymnastics, and so on.

Such activity is not indicated for those 30 or more pounds overweight. They must be content to walk quietly, first on level ground, that gradually on steeper ground until they can undertake hills and mountains and get some real exercise. For those whose weight exceeds the optimum by 45 pounds physical exercise must be prescribed with extreme caution; in general their fat should be reduced by other means.

This brings us finally to diet and reduction.

If a man's ideal weight is 150 pounds and he does light work, 2600 calories daily is sufficient energy intake. A "maintenance diet" is one upon which he neither gains or loses weight. He should have in that diet about 50 grams of protein (nearly 2 ounces) at least though a better diet would be 90 grams of protein, 75 of fat, and 375 of carbohydrates.

All reducing diets are calculated on a basis of the caloric value of the maintenance diet. One ounce of human fat is worth 279 cal-

ories in heat and energy. Hence a diet that is less than the maintenance diet by 558 calories will result in a daily loss of 2 ounces or 14 ounces reduction per week. To lose 2 pounds a week the maintenance diet would have to be cut by 1275 calories; to lose 4 pounds a week it would have to be reduced by 2551 calories—which would leave only 49!

Because fat is deposited slowly its rapid removal is unwise. Long fasts or extremely poor diets are ill-advised though a person can lose 10 to 12 ounces a day in moderate activity if he eats nothing at all. Fasts of longer than one week duration are dangerous even for the strong and healthy. Short fasts may be used, however, to inaugurate courses in weight reduction.

A relative fast may be achieved by taikng the juice of one orange on waking, weak tea with 2 tablespoonfuls of skim milk for breakfast, a little veal broth for lunch, the weak tea and milk again in the afternoon and 4 ounces of breast of chicken with lettuce and celery for dinner. This diet is worth 266 calories of which only 3 grams is fat.

The following is a good "starvation diet," worth only 160 calories: 10 ounces of water on waking; one-half grapefruit and tea with 1 ounce of milk for breakfast; 10 ounces of water at 11 A. M.; clear bouillon for lunch with a small orange; tea with 1 ounce milk in the afternoon; one-half grapefruit and bouillon for dinner and 10 ounces of water at bed time.

If it is desired to step this up to about 534 calories add 4 ounces of steak, mutton or fish at lunch time with 4 ounces of some green vegetable and the same at dinner. But remember that even "semi-starvation" diets containing 750 calories do not carry enough nutriment to be depended upon for very long.

Diets that reduce weight slowly and are safer contain from a thousand calories, to over twelve hundred. To obtain the calorie value of a diet on which 2 pounds of fat may be lost per week deduct 1275 calories a day from the maintenance diet: i. e. 2600 calories—1275 equals 1325 calories the diet may contain.

Then keep in mind that the usual 4-ounce helping of lean beef (grilled) is worth 175 calories, of roast leg of veal 145; that 3½ ounces of cauliflower or brussels sprouts will add 11 and 17 calories respectively; that two helpings of salad run about 64, one medium-

size pear about 55 and one medium-size apple about 62, while a glass of skim milk contains 71 calories.

Allocate the foods to the meals desired. Count the calories gain. Allow always just as little fat as possible but make the protein allowance generous. If you simply have to then allot one-eighth of the energy value of the diet to alcoholic beverages and always remember they constitute food. Watch the vitamins!

For the 150-pound sedentary man the 1325 calories should be composed of 104 grams of protein, 30 of fat, and 151 of carbohydrates. If he takes 2 whiskies and sodas the balance is altered to—104 grams of protein, 30 of fat, 111 of carbohydrate, and 23.4 grams alcohol—which is food, like it or not.

Avoid all patented trick weight-reduction diets just as you avoid drugs and patent obesity cures.

The Fate of Erythritol and Erythritan in the Animal Body. F. F. Beck, C. J. Carr and J. C. Krantz, Jr. *Quart. J. Pharm. & Pharmacol. 11,* 234 (1938). The authors have previously reported on a metabolism of various sugar alcohols. In this paper a study of erythitol and its anhydride erythritan is reported in which both were given to white rats orally and injected intraperitoneally. When orally administered (4 cc. of a 10 per cent. solution) these substances were excreted unchanged in the urine, a recovery of between 20-40 per cent. being made during a 4-5 hour period. No significant effect was observed on the respiratory quotient or the oxygen consumption. No addition or significant decrease in the stores of liver or tissue glycogen were found.

Intraperitonial injections gave rise to definite toxic symptoms which were considered to be due only to osmotic effects. L. F. T.

ABSTRACTS FROM AND REVIEWS OF THE LITERATURE OF THE SCIENCES SUPPORTING PUBLIC HEALTH

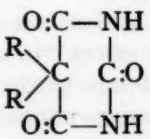
Bacteriology . . . . Louis Gershenfeld, B. Sc., Ph M.
Biochemistry, Nutrition, etc. . . . Arno Viehoever, Ph. D.
Biology . . . . . Marin S. Dunn, Ph. D.
Chemistry . . . . . Arthur Osol, Ph. D.
Pharmacy . . . . . E. Fullerton Cook, Ph. M.
and their assistants

COMPARATIVE VALUE OF THE BARBITURATES

By Horatio C. Wood, Jr.

IT IS nearly thirty years since diethylmalonyl-urea was introduced as a somnifacient, under the trade name of Veronal. It achieved very rapid popularity, and in a few years became the most widely used of hypnotic drugs. The success of this drug naturally stimulated other manufacturers to produce allied compounds, and during the past decade there have been introduced, and vigorously advertised to the doctors of this country, more than a dozen closely related chemicals.

The great majority of the drugs of this group are aliphatic derivatives of malonyl-urea (barbituric acid), differing only in the aliphatic side radicals.



GENERIC FORMULA OF THE BARBITURATES

In Barbital both of the "R"s are ethyls (C_2H_5); in Phenobarbital one R is an ethyl and the other a phenyl (C_6H_5). The unofficial drugs of the series contain various other side groups.

Recently there has been some experimentation with compounds in which the atom of oxygen in the urea group has been replaced by an atom of sulphur, forming the thiobarbiturates. At least one of these is being used to a considerable extent.

Although barbital is often referred to as diethylbarbituric acid, it will be noted from the above formula that it contains no carboxyl group, and is therefore not an acid in the usual concept of organic acids. It is capable, however, of combining with sodium, the metal probably being attached to the oxygen in the form of a lactim. The sodium combination is soluble in water in contrast to the barbital, and has an alkaline reaction. The aqueous solution, however, is rather unstable, a large part taking up a molecule of water by hydrolysis and forming diethylmalonuric acid. This new compound does not possess the narcotic powers of barbital.

All of the barbituric series apparently have similar chemical properties. Most of the unofficial ones are marketed as sodium compounds.

Before we start to consider the choice between the various members of this group it is necessary to note that their usefulness has extended far beyond the field that was dreamed of by the introducers of veronal. Not only are various members of this group used to overcome insomnia but they are also used to relieve general nervous excitability, to help quiet headache, in the treatment of epilepsy, to allay the convulsions of strychnine or cocaine poisoning and as anesthetics for major surgical operations. It is obvious that quite different criteria would influence our choice of a drug to be used in an acute emergency such as surgical anesthesia, as compared to a chronic complaint like epilepsy.

There is little difference between the physiological effects of the various members of the barbiturates. In moderate doses their dominant action is upon the cerebrum, producing a partial loss of consciousness closely approximating normal sleep. With increasing doses the narcosis becomes more and more profound, until the patient passes into a condition of complete coma, insensible to any sort of external stimulus. With the small, or hypnotic, dose there is a slight fall of the blood pressure, due to a dilatation of the peripheral blood vessels, and some increase in the permeability of the capillaries (which becomes of importance after toxic doses); there is also a slight reduction in the basal metabolism and in the blood

calcium, but not notably greater than after other hypnotics. The heart is not much affected, indeed even fatal doses produce comparatively slight cardiac changes. The respiration may be slightly diminished; after large doses it is greatly depressed, and in many cases of fatal poisoning death is due to respiratory failure. (It may be noted in passing that there are two types of fatalities caused by the barbiturates, one the acute death from cessation of breathing, and the other occurring after some days and apparently due to the injurious effects upon the capillary blood vessels which lead to edema of the lungs and to hemorrhage in the central nervous system and other internal organs.) Small doses have little effect upon the sensory apparatus—although they do enhance the analgesic action of other anodynes—nor upon the motor centers of the spinal cord; large doses completely abolish all sensation and all reflexes.

In choosing between these drugs the first question that would naturally come into our mind is, which is the least dangerous? A large number of attempts to answer this question have been made by comparing the doses required to produce therapeutic effect to those which are likely to prove fatal. At first sight this would seem a very reasonable way to determine the relative safety of the members of any group of closely related drugs, but there are certain practical obstacles which have greatly lessened the value of the industrious researches which have been made along these lines. In the first place the degree of narcosis is something which it is almost impossible to evaluate accurately. Secondly, the toxic dose varies, as with all drugs, according to the channel of administration, but not to the same degree. For instance, Fitch and Tatum have shown that the fatal dose of phenobarbital by mouth is almost the same as that by intraperitoneal injection, but with amytal it requires more than six times as much to kill by mouth as it does by injection. In the third place, we are dealing with comparatively slight differences in toxicity. From a careful review of the papers comparing the lethal and therapeutic doses which have been published the most justifiable conclusion that can, in our opinion, be drawn is that the barbiturates may be arranged into three groups as far as their toxicity is concerned. In the first division (least dangerous) may be placed Seconal, Dial, Pentobarbital, Amytal, and Phandorn; in the middle belong Neonal and Pernostal, while Ipral, Barbital and Phenobarbital are apparently decidedly more toxic than the above.

In 1932 Fitch and Tatum suggested a new criterion for comparative evaluation of different barbiturates based not on the relationship between lethal and therapeutic dose but upon the duration of the narcosis produced. This standard of comparison is of real practical value. For instance, if we have a condition of epilepsy where it is necessary to keep the patient in a very mild depression continuously for weeks and months, obviously we want a drug whose action is very slow. On the other hand, in the emergency of strychnine poisoning or for surgical anesthesia we want a drug whose action is powerful and short.

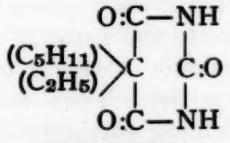
We may divide these drugs into four groups according to the duration of their effects. In the ultrashort actors are Evipal and Pentothal. The second group would include Seconal, Dial, Pentobarbital, Amytal, Pernostal and Phanodorn; somewhat more prolonged in their effects are Alurate, Ipral and Neonal, while the long actors are Barbital and Phenobarbital.

The reason for the difference in the duration of the effects of these various drugs is probably to be found in their mode of excretion. While it has not been experimentally proven, except for one or two of them, it is generally believed that all the short actors are broken down in the liver—a process which is comparatively rapid—while phenobarbital and barbital are not broken down in the body and continue to circulate in the blood until they are excreted by the kidneys. After the administration of barbital, 85 per cent. of the ingested dose can be recovered from the urine, but after amytal, practically none appears in the urine.

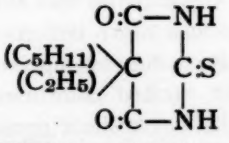
A special word may be in place concerning two recent members of the family, evipal and pentothal, which are at present attracting a great deal of attention as surgical anesthetics. Their value for this purpose lies in the extraordinary rapidity of their action, a feature which militates against their use as hypnotics or as general nervous sedatives.

Many of the barbiturates have been used in surgical anesthesia, sometimes as the sole anesthetic, more commonly as a "basal anesthetic". By this latter term is meant a drug which is used preliminary to some inhalation anesthetic, as nitrous oxide or ether, the claimed advantages being that not only is the patient spared the nervous excitement of ether anesthesia, but a much smaller quantity of the anesthetic will be required, and the post-operative convalescence

correspondingly less distressful. The disadvantage of using a non-volatile drug as sole anesthetic agent in major surgical anesthesia lies in the fact that it is impossible to foresee in any individual case just the exact quantity of drug which will be required to carry the patient through the operation, and if by any chance the subject is abnormally susceptible to the drug there may develop serious or possibly fatal poisoning, whereas with nitrous oxide or ether the depth of the anesthesia can be nicely regulated from minute to minute. Even with the short actors like Amytal or Seconal, whose effects will last two or three hours, it is obvious that their chief value in surgery will be as basal rather than sole anesthetics. According to the studies of Dr. Tatum, when given intravenously in 60 per cent. of their respective lethal doses, the narcosis after Evipal is less than one-third as long as after Pentobarbital, and that of Pentothal is still shorter. Both of these drugs have been used by intravenous injection in surgical anesthesia in thousands of cases. A German writer, named Baetzner, in 1935 estimated the number of Evipal anesthesias in Europe at one and one-half million, and stated that there were only sixty anesthetic deaths in that group, a mortality rate which compares very favorably with that of ether. The same writer warns, however, that in cases of disorders of the liver or impaired circulation the drug is much more dangerous.



PENTOBARBITAL



PENTOTHAL, a thiobarbiturate

As mentioned above, Pentothal differs materially from the drugs we have been considering in that it has sulphur in its molecule. There is considerable experimental evidence that it differs physiologically in that it exerts some deleterious influence directly on the heart. There is not yet sufficient data to allow a final decision as to whether this cardiac effect is important enough to render the drug unduly dangerous as a general anesthetic. It may be remarked in passing that even if intravenous anesthesia by these drugs should largely replace that by inhalation, the expert anesthetists will not

be thrown out of employment, because the proper and safe intravenous anesthesia demands a degree of skill which is certainly not less than that required in the administration of ether.

The Acidimetric Titration of Ergometrine. F. Reimers. *Quart. J. Pharm. Pharmacol. 11,* 252 (1938). As with the majority of ergot alkaloids and their salts ergometrine crystallizes with fairly large and varying quantities of the solvent and this is so firmly combined that it can only be removed entirely by heating *in vacuo.* Consequently, the content of specimens of ergometrine on the market may vary in a fairly largely degree and a method of determining the ergometrine content is important. Dudley (*Proc. Roy. Soc. Ser. B 118,* 478 (1935) showed that ergometrine behaves as a monacid base which forms well defined salts with one equivalent of acid. The author has investigated the possibility of determining the ergometrine content by a simple acidimetric titration with satisfactory results. The method is as follows: A test is first applied to determine the possible presence of other ergot alkaloids. 2 cc. of a solution of the sample containing 2 mg. is treated with 2 drops of diluted hydrochloric acid and 5 drops of 1 per cent. aqueous picric acid. The appearance of an opalescence or precipitate indicates the presence of 2 per cent. or more ergotoxine or ergotamine in the sample of ergometrine.

When ergometrine was titrated electrometrically with n/10 hydrochloric acid a sharp deflection in the curve was found at pH 4.4. Consequently, using bromphenol blue indicator a sample of ergometrine was titrated colorimetrically to a bluish green end point giving results in excellent agreement with those obtained by drying the sample *in vacuo.* In dissolving the sample in water it must be heated on a water bath some time and care must be taken that it does not adhere to the sides of the glass as a translucent mass.

On account of the high cost of ergometrine a microtitration procedure is described which requires only a 5-10 mg. sample.

L. F. T.

Report on Drugs. L. E. Warren. *J. A. O. A. C. 21,* 519 (1938). In the following report Dr. L. E. Warren of the U. S. Food & Drug Administration, has summarized reports of the several associate referees on the analyses of drugs. This report is re-

printed here that those interested in some specific phase of this work may refer to the detailed report in the same journal. A. O.

"Since the last meeting there have been two occurrences which are of interest to drug analysts:

(1) The first supplement of the U. S. P. XI appeared in August. It becomes official December 1, 1937. This is a brochure of 104 pages. It contains no strictly new topics, although permission is granted to use water other than distilled water in the manufacture of certain products.

(2) The second list of corrections for the National Formulary VI was issued in early summer. To date there has been no interim revision of the National Formulary VI, but there is a possibility that a new edition will be published about 1940.

Last year 26 topics were assigned to associate referees and another topic was added after the meeting. Substantial progress has been reported in 24 subjects. From these reports the Referee is able to recommend for adoption chemical methods for the determination of five substances, viz., cinchophen in presence of salicylates, homatropine in tablets, pyridium, and caffeine and potassium bromide in effervescent mixtures. Further, he is able to recommend the adoption of tentative microchemical methods for the identification of seven substances; viz., apomorphine, ethylmorphine, benzylmorphine, hydrastinine, benzoic acid, salicylic acid, and acetylsalicylic acid.

Last year attention was called to the fact that the Association is now studying directions for preparing and standardizing certain volumetric solutions. The Association has a referee on the subject. Although all of the volumetric solutions described in *Methods of Analysis* do not come within the purview of the Drug Section, many do, and such information is naturally of much interest to drug analysts. Among the solutions so prepared and standardized are sodium hydroxide, hydrochloric acid, and alcoholic potassium hydroxide, aldehyde free. Undoubtedly standardization methods for other volumetric solutions will be adopted from time to time.

Microchemical Tests for Alkaloids.—Previous to this year the Association had adopted one or more microchemical methods for the identification of 29 alkaloids, including a few synthetics having alkaloidal properties. This year apomorphine, hydrastinine, ethylmorphine (dionine), and benzylmorphine (peronine) were studied. Last year, *This Journal, 20,* 55 (1937), the Association recommended that

berberine and cytisine be studied also. Supplies of cytisine could not be obtained, and the preliminary tests on berberine were not sufficiently good to warrant collaborative tests. The observation by Shupe that apomorphine hydrochloride is precipitated by hydrochloric acid was confirmed, but it was found that benzylmorphine also reacted in the same way. The microchemical tests submitted to the collaborators gave satisfactory identifications. The associate referee recommends that the microchemical tests for hydrastinine, ethylmorphine (dionine), benzylmorphine (peronine), and apomorphine be adopted as tentative. He further recommends that the topic be continued to include berberine, coniine, narcotine, and narceine; also cytisine if available. The Referee concurs.

Microchemical Tests for Synthetics.—Previous to this year the Association had adopted microchemical methods for the identification of 15 synthetic substances in addition to several synthetics that have alkaloidal properties. The subject of microchemical tests for synthetics is such a large one that it may be said that the Association has only just started in its studies of this topic. This year microchemical methods for acetylsalicylic acid, benzoic acid, and salicylic acid were studied. No report was submitted on diallyl barbituric acid which Subcommittee B recommended for study last year. The associate referee recommends that the microchemical methods for each of the substances that were studied collaboratively be adopted as tentative. This is approved. The associate referee further recommends that "other important synthetics be studied." The Referee recommends that sulfanilamide, mandelic acid, and diallyl barbituric acid be studied.

Hypophosphites.—The bromine oxidation method was studied by the associate referee this year. Good results were obtained in the analysis of commercial sirup of hypophosphites but no collaborative work was done and no samples of known composition were prepared and assayed. The associate referee recommends that the bromine oxidation method be subjected to collaborative study. The Referee concurs.

Santonin, Phenolphthalein, and Calomel in Tablets.—Last year the collaborative results for the determination of santonin and calomel were good, but several collaborators reported high values for phenolphthalein. This year the work was confined to the separation and determination of phenolphthalein in such mixtures. The

results were somewhat erratic. The associate referee recommends continuation of the topic. This is approved.

Daphnia Methods.—The associate referee has continued his studies on the application of daphnia to the evaluation of various drugs such as laxatives, pilocarpine, strychnine, and certain vitamins. He recommends that the topic be continued. The Referee concurs.

Determination of Hexylresorcinol in Olive Oil Solutions.—A tentative method for the determination of hexylresorcinol was adopted last year, *This Journal, 20,* 81 (1937). The topic was continued to include determination of the substance in preparations. The associate referee has developed a method in which oxidation is prevented by hydrazine. The associate referee and two collaborators obtained good results in assays of one known specimen of hexylresorcinol in olive oil. The associate referee recommends that the subject be continued in order to obtain more collaborative results and to extend the method to other preparations containing hexylresorcinol. The Referee concurs.

Ergot Alkaloids.—This topic has been studied for several years. Last year the total alkaloids were extracted in an automatic extractor; this year by the hand separator. The latter method does not secure complete extraction. Since the problem appears to be in its preliminary stages the associate referee recommends its continuance. In this the Referee concurs.

Nitroglycerin in Mixtures.—The associate referee continued his work of last year and reports the results from two collaborators as well as his own findings. The double distillation method gave consistent results on tablets (whole and powdered), but in complex mixtures the results were low. The Referee recommends that the subject be continued.

Guaiacol.—The associate referee devised a method for the determination of guaiacol that depends on the determination of the methoxy group. He applied the method to guaiacol and to guaiacol carbonate and found it satisfactory. However, he has been unable to submit the method to collaborative study. The Referee recommends that the subject be continued.

Biological Testing.—The associate referee reports that no work was done. It is recommended that the topic be continued.

Iodine Ointment.—The associate referee and his collaborators tried methods for the determination of free iodine and for organically

combined iodine. The method for free iodine was found satisfactory and is recommended for tentative adoption. The method for organically combined iodine was not satisfactory. The associate referee recommends that the subject be continued. These recommendations are approved.

Aspirin, Acetophenetidin, and Caffeine in Mixtures.—This topic has been studied for several years. According to a preliminary report, this year the associate referee devoted his energies particularly to the separation and recovery of caffeine, but no method was developed sufficiently well to warrant collaborative work. The associate referee's recommendation that the subject be continued is approved.

Pyridium.—The associate referee worked out a method for assaying pyridium (base) in jellies, ointments, and tablets. The method is an application of the titanium chloride titration for certain dyes. Good results were obtained by the associate referee on knowns, but little collaborative work was done. The recommendation of the associate referee that the proposed method be studied collaboratively is approved by the Referee.

Gums.—Methods for the identification of gums, either singly or in mixtures, have been studied for three years but none has been adopted. Methods developed for the identification of single gums were moderately satisfactory, but they were totally inadequate when applied to mixtures. Furthermore, the reactions observed for pure commercial gums (unmixed with other substances) did not correspond with those obtained by the residues after the gums had been separated from pharmaceuticals. This year no work was done. The Referee is of the opinion that the topic should be continued.

Cinchophen in Presence of Salicylates.—The associate referee applied the well-known Emery method to this problem. The results obtained by each of the collaborators were good. The associate referee recommends that the method subjected to collaborative study be adopted as tentative and that the subject be closed. The Referee concurs.

Theobromine Calcium Tablets.—The Association has adopted a periodide method for the assay of theobromine in theobromine calcium. This year the associate referee and his collaborators studied theobromine calcium tablets. (The method used is an adaptation of the silver nitrate procedure of Boie.) They also applied the method

of pure theobromine and to theobromine calcium powder. The results are in good agreement. The associate referee recommends that the Boie method be adopted as tentative to supersede the periodide method already adopted. This recommendation applies to theobromine also. The Referee is of the opinion that the Boie method should be adopted as an alternative tentative procedure, but that the adoption of the periodide method should not be rescinded, and he so recommends. The associate referee recommends that an application of the method to theophylline be studied. The Referee doubts the wisdom of this action at this time since the U. S. P. XI and the A. O. A. C. have each adopted a method for the assay of theophylline.

Chlorbutanol.—The associate referee has applied a distillation method to products containing known amounts of chlorbutanol, with subsequent conversion of the chlorine to chloride by alcoholic potassium hydroxide in a pressure bottle. The collaborative results were not entirely consistent. The associate referee recommends that the subject be continued. The Referee concurs.

Aspirin and Phenolphthalein Mixtures.—This subject has been under consideration for three years. Last year the associate referee applied the Hitchens method, *J. Am. Pharm. Assoc., 23,* 1084 (1934), to a mixture of phenolphthalein, acetylsalicylic acid, and starch. His results were promising, but the findings by the collaborators were disappointing. This year the collaborative results were still unsatisfactory. The recommendation of the associate referee that the subject be continued is approved.

Homatropine in Tablets.—This subject has been studied for two years. Last year the associate referee found that the tentative A. O. A. C. method for atropine in tablets, *Methods of Analysis,* 1935, 555, gave reasonably good results for homatropine, but no collaborative work was done. This year the method was subjected to collaborative study with good results. The associate referee recommends the method for adoption as official, first action. Although it is somewhat unusual to adopt a method as "official, first action" without the method having passed through the tentative adoption stage, it may be justifiable in this case since the method is a standard one for other alkaloids and since it gave good results in the hands of the associate referee last year. The Referee concurs with the recommendation of the associate referee.

The associate referee has devoted a great deal of time to the search for a method of separating homatropine from cocaine but without success. He recommends that the subject be closed. The Referee concurs.

Cubeb.—An assay method for cubeb has been studied for two years. The method used is an adaptation of the method for volatile oils in spices, *Methods of Analysis,* 1935, 447. Last year the National Formulary adopted an assay method for cubeb. This is a determination of "Volatile Ether Extract" and differs greatly from the A. O. A. C. method.

Since the N. F. VI method and the A. O. A. C. method are different in principle, it was decided last year to continue work on cubeb. The associate referee reports good results with the method sent out for collaborative study. His recommendation that his method be adopted as tentative for cubeb is approved. He further recommends that the subject of cubeb be closed and that cardamom be studied. Both of these recommendations are approved.

Aminopyrine and Phenobarbital in Mixtures.—The associate referee devised a somewhat empirical method of separation by which the aminopyrine is removed by chlorofrom from an aqueous alkaline solution. Afterward the aqueous solution is acidified and the phenobarbital is removed by ether. The results were reasonably satisfactory. It is recommended that the subject be continued to include collaborative work.

Effervescent Potassium Bromide with Caffeine.—The associate referee and his collaborators have applied well-known analytical methods for the assay of bromide and caffeine to this product. The results are excellent. The associate referee reports that caffeine cannot be dried for long periods at 100° C. without slight loss. He recommends drying at 80° C. His recommendations, that the methods submitted to collaborative study be adopted as tentative, are approved.

Elixir of Terpin Hydrate with Codeine.—The A. O. A. C. has adopted a method for the assay of elixir of terpin hydrate but none for codeine, if present in the elixir.

The associate referee and his collaborators have used a method for the determination of codeine, which was elaborated by several other Association chemists. The results for codeine were reasonably good but for terpin hydrate only fair. The recommendations of the

associate referee that the method used be adopted as tentative for codeine in elixir of terpin hydrate and codeine is approved.

Emulsions of Cod-liver Oil.—Various methods of extracting the oil from emulsions were tried by the associate referee. These included shaking out with chloroform in a separator, and extraction with chloroform in a Soxhlet apparatus. Neither the Mojonnier tube nor the Roese-Gottlieb method in a Röhrig-Biesterfeld tube (*J. Ind. Eng. Chem., 9,* 1111 (1917); *Methods of Analysis, A. O. A. C.,* 1935, 267) was tried. The Referee has used these methods on emulsions of liquid petrolatum with satisfactory results.

The associate referee recommends that the topic be continued. The Referee concurs.

Ointment of Mercuric Nitrate (*Citrine Ointment*).—This is a new topic. The associate referee has applied a modification of the thiocynate method to this product. The results, in general, were somewhat low. The Referee suggests that this may be due to insufficient melting and washing. The method, as sent to the Referee for collaborative study, made but one melting of the fatty material. The associate referee is aware that his proposed method gives low results, but he is of the opinion that, since citrine ointment is a subject of small importance in pharmacy, the topic should be closed.

Since so much work has already been done, the Referee is of the opinion that the topic should be continued for one more year.

Rhubarb and Rhaponticum.—This topic has been under consideration for a number of years. Some interesting reports have been published, but they have not resulted in the adoption by this Association of any methods for distinguishing between the two drugs. This year the associate referee attempted to secure authentic specimens of rhaponticum for study and reviewed the subject from the published data. To date he has not secured supplies but contacts with importers are in progress. His recommendation that the topic be continued is approved.

Theophylline Sodium Salicylate.—Last year, *This Journal, 20,* 82 (1937), the Association adopted a method for the assay of theophylline that is applicable to most preparations of the drug such as solutions, tablets, etc. The process consists in dissolving out the alkaloid from its preparations with sodium hydroxide, acidifying the solution, and shaking out with a mixture of chloroform and isopropyl alcohol. The method was not tried on theophylline sodium salicylate

for the reason that it might not be expected to work on this preparation due to the liberation of free salicylic acid during the procedure. This would be extracted and weighed as theophylline (with danger of loss due to volatility).

This year the associate referee devised a clever method of separation based on the differing solubilities of salicylic acid and theophylline in different mixtures of solvents. He also devised a volumetric silver precipitation method for theophylline, after which the salicylic acid is determined by the official A. O. A. C. method, *Methods of Analysis,* 1935, 551. The associate referee recommends that both methods for theophylline be adopted as tentative for theophylline salicylate. He further recommends that the methods when applied to mixtures with excipients be studied further. The Referee believes that further work should be done and so recommends.

Sulfanilamide.—This compound has recently come into use as a treatment for infections with beta-hemolytic streptococci. Methods for its evaluation have been proposed but have not been considered by the Association. It is recommended that sulfanilamide be studied.

Mandelic Acid.—During the past few years mandelic acid and its salts have come into extended use in the treatment of certain infections. It is recommended that mandelic acid and its salts be studied.

Arecoline Hydrobromide.—Arecoline hydrobromide is being used considerably in veterinary medicine. No methods of assay for the product from the alkaloidal standpoint are provided in the various compendiums. It is recommended that the subject be studied."

A Rapid Method for the Isolation of Organic Poisons. C. P. Stewart, S. K. Chatterji and S. Smith. *Brit. Med. J. 2,* 790 (1937) through *Quart. J. Pharm. & Pharmacol. 11,* 293 (1938). The customary tedious method for the isolation of organic poisons from animal tissues may be replaced by the simple method of grinding with an equal volume of 10 per cent. trichloracetic acid, and then filtering, whereby a water-clear solution is obtained, practically free from fat and protein and containing any alkaloids present in the original material together with any other basic material, water soluble non-basic substances and most glycosides. This solution may now be shaken with kaolin, which adsorbs the alkaloid and the separated kaolin washed once with water, ground with sufficient 10 per

cent. sodium carbonate solution to make the suspension alkaline mixed with anhydrous sodium sulfate to give a dry powder and then extracted in a Soxhlet apparatus with chloroform. In experimental extractions the recovery of strychnine by this process was 88 and 97 per cent. of substance which was pure as shown by its physical and chemical properties. One mg. of strychnine mixed with 400 gm. of minced meat was recovered in sufficient quantity to give the sulfuric acid-potassium dichromate test.

Equally good results were obtained with morphine and quinine and qualitatively satisfactory with nicotine and aconitine but the method has not yet been fully explored. The kaolin used in the elution of the alkaloid should be washed with alcohol, chloroform, and finally with ether before being used as otherwise some color may be yielded to the chloroform extract after adsorption. L. F. T.

Silica Gels as Ointment Bases. Peronnet and Genet. *J. Pharm. Chim., Paris, 26,* 490 (1937) through *Quart. J. Pharm. & Pharmacol. 11,* 315 (1938). The use of a silica gel as an ointment base is suggested. The gel is prepared by adding, drop by drop and with constant stirring, commercial solution of sodium silicate, diluted with three times its volume of water to hydrochloric acid until the mixture assumes a vitreous appearance; this occurs when the volume of the diluted silicate solution added is about twelve to thirteen times that of the hydrochloric acid. The mixture which is slightly alkaline is filtered and washed rapidly on a Buchner funnel. The gel obtained is of a desirable consistence but in this form it is not stable. By titurating the gel with a quarter of its weight of glycerin a homogeneous product resembling soft paraffin is obtained which when kept in closed containers remains stable over several months. It readily absorbs vegetable oils and is readily miscible with a large number of medicaments but not with hydrocarbons. Ointments of boric acid, camphor, red mercuric oxide, phenol, etc., can be prepared with the gel as the base. Iodine, certain mercuric compounds (including the yellow oxide) polyhydric phenols and acids are incompatible with it.

As an ointment base the gel has the advantages that it is non-irritant to the skin, is non-greasy and can be readily removed by washing even with cold water. Whether the properties of the medicaments of such ointments are influenced by the base is yet to be ascertained. L. F. T.

SOLID EXTRACTS

By Ivor Griffith, Ph. M., Sc. D.

Despite the form in which this information is presented it may be accepted as trustworthy and up-to-date. Original sources are not listed but they may be obtained upon request.

Said a glib schoolboy, "Science is material and religion is immaterial." John Fiske, the natural and nature-loving Scotchman, said just the opposite. And when we consider the fact that our conception of time and distance is very limited indeed, we should remember also that all of our scientific findings are based on finite premises. We know no more today, of the riddle of the universe than does a moth, bewildered by the glare of the tungsten glow, know of the flow of the electric fluid. And science has mothlike flapped its flimsy wings in fruitless search for the secret of this same electric force that so confounds the little moth.

Perhaps we should be patient, for evolution is forward functioning, not just a tool of the past and it may be that with constant experiment, we shall yet learn many of the now obscure facts.

In the meantime, we must be willing to agree that

"All of philosophy is only a rhyme
And Science a vaporous wraith
Man's only hope for a conquest of Time
Is a simple reliance on Faith."

And although we acknowledge and admit these limitations of the human mind, there are times, with all of us, when the ego needs an astringent. By far the best astringent for such a swollen ego is the tannin of contrast, which if properly applied shrinks and shrivels a perfectly capital I to the knee-bent lower case. Let conceited man think of himself not in contrast to the atom, the cell, the worm, the gnat, the ant, but rather in contrast to stars.

Let him remember that the milky way, to the naked eye, a smear in the starlit sky, consists of millions upon millions of stars, contrasted with which our Sun, a giant compared with our Earth, is but a midget. Antares, the largest star yet measured, has a diameter of 400,000,000 miles; the Earth has a diameter of 8,000 miles.

Still, in the depths of space are untold numbers of other systems, many of them, incredibly, larger than our own. Should, perchance, the Earth collide with one of these celestial bodies, it would mean annihilation of the Earth in the wink of an eye.

Therein lies the great futility of our positiveness and the nonsense of our conceit.

Dr. Henry Leffmann of Philadelphia used to remark that the therapeutic graveyard was a splendid place for research. And why not? For here are buried a host of drugs, and like the glorious kings of Egypt—with their properties buried beside them.

Truly enough, there are many such drugs, that should remain buried, and the night-prowling, carcass-hunting scientist, will do well to leave them alone. There are enough good ones to resurrect.

Read the towering memorials in the medicinal graveyard and recollect the heydey of some of these well-dead drug-duds. There is the tall monument sacred to the memory of Friedman's Turtle Serum; and an obelisk to Koch's Tuberculin Treatment—and there are stones of less significance to a myriad dead chemicals, dead processes, dead botanicals and dead zoologicals.

Read them as you amble down the grassy aisles, Sassafras, smilax, snakeroot and salicin; bloodletting, cupping, leeching and baths; syrup of zoo, essence of spittle, wine of ear wax, tincture of toes.

Truly this is a graveyard!

Yet I repeat that here lie prematurely buried a host of drugs deserving of a better destiny. In a mad scramble to squeeze out of the coal tar barrel every available virtue, research has neglected the botanicals.

No child disease is as depleting and exasperating to both patient and parent as the wild and noisy pertussis (whooping cough). Difficult to control and frequently fatal, it at last shows signs of surrender. For vaccination against whooping cough got a good rating recently in a report by Dr. Pearl Kendrick of the Michigan State Department of Health and Dr. Anthony K. Borowski of Mount Clemens, Mich.

The number of cases that developed in 1815 vaccinated children was 52, whereas, there were 348 cases among 2397 unvaccinated children. When vaccinated children did get whooping cough they had less severe attacks than the unvaccinated children.

To which we say, with becoming dignity, "Whoopee!"

"To abuse snuff," says Coleridge, "is to abuse the origin of the human nose." But snuff has gone the way of most Victorian luxuries, as the parlor stereopticon and whatnots and antimacassars and family albums. Yet it has its devotees, and some use has to be made of dust and sweepings from cigar factories. It will be a surprise to know that twenty-five million dollars' worth of snuff was manufactured in America in 1936, most of it, however, for export elsewhere, possibly to Sweden as Swedish snuff, or to the Land of MacTavish and Fergusson as Scotch Snuff—in return for some of Scotland's courtesies.

Snuff sniffing, once a most popular pastime, is said by some to be due to return to its catarrhal haunts.

It might be an interesting poser for even Professor Quiz himself were he asked the location, on the anatomic landscape, of that little spot termed the snuff box. It is at the backhand base of the thumb, seen as a depression, when the thumb is bent and rigid! This is where the snuff-sniffer placed his little mound of snuff prior to its insufflation.

And speaking of tobacco, John Brown judges his cigar—as he does a great many other things—by the cover—and by way of paradox, it might be said—that in so judging it he misjudges it.

A leaf grown in light sandy soil or very light loamy soil, with clayey subsoil, usually affords a light yellow tobacco. Heavily manured soil produces a dark heavy leaf. Yet the color is no indication of the strength of the leaf—for while a dark leaf, not necessarily strong, can not be bleached without injuring its flavor, yet a light leaf, possibly strong in constituents, may be very readily darkened by processes subsequent to growth.

It is the heart of the cigar—the filler—that regulates the potency and pungency of the smoke—the wrapper is only for ornament

and for protection, and only constitutes a very small percentage of the weight of the cigar.

That man has in the field of textile staples reached the "creative" age is now a certainty. It is a long day, since Eve, in Eden suburbs, conscious of new sensations, both of shiver and shame, made herself a garment of leaves. From that acquisitive day when primitive peoples used what they found afield, through the adoptive stages when man modified natural products, in textiles, by felting and spinning and weaving, to this the creative age progress has been slow but very certain.

And now we have new fibers and rumors of fibers made, not from animal fur or vegetable filament nor from the cocoon's silken shroud, but actually from coal, water and air.

Nylon, the new and definite synthetic Dupont fiber, can be fashioned into filaments, steel-strong, yet fine as the spider's web. It is elastic and lustrous, and superior to all known natural fibers in toughness and tensile strength.

Some of our medical historians have attempted to explode, as a myth, the oft-recurring statement that syphilis was the curse inflicted by American Indians, in return for the white man's introduction to them of the dreaded tuberculosis. On the same basis they exchanged with him, their tobacco for his firewater.

It is interesting to read from a book contemporary almost with Columbus (Diaz de Isla (Ruy) of Baeza, 1542, *Contra el mal Serpentino*) *the following translation: "Of the origin and birth of this serpentine disease of the Island Hispianiola. The disease appeared and was seen in Spain in the year 1493 in the city of Barcelona; the which city was infected and in consequence the whole of Europe, and the universe of all known countries which are within reach of one another; the which evil had its origin and birth of old in the Island which to-day is called Hispaniola; this island was discovered and found by the Admiral Don Christobal Columbus and up to the present there has been intercourse and communication with the people there."*

BOOK REVIEWS

Done by persons, unafraid to upbraid, but perfectly willing to give praise where praise is really due.

Methods of Analysis for Medicinal Specialties. Compiled by the Specialties Commission of the International Pharmaceutical Federation, 2nd Ed. in German, 148 pages, 10 illustrations. Published 1938 by Dekker and Nordemann, Amsterdam. Price fls. 3.50, Reich Mark 5.00.

The commission, consisting of van Itallie, The Hague, President; Rasmussen, Copenhagen, Secretary; Herissey, Paris; Rising, Stockholm; Weis, Vienna; Casparis, Berne; Rojahn (†) Halle a. d. S.; and Madsen, Copenhagen, presents herewith the results of a revision and extension of the book, published five years previously. The brief description of general methods of analysis, as that of melting, boiling and freezing-points, of the refractive index, viscosity, total and acid insoluble ash, extractive substances and of alcohols, is followed by naming of rules for carrying out reactions for identity and purity, by the statements of the procedure for destruction of organic substances, and of the detection as well as determination of those elements and compounds, including tablets, occurring, as a rule, in specialties.

Numerous tabulations throughout the book, as well as lists of special reagents, buffer solutions and indicators, not mentioned in the text, greatly increase the usefulness of this book of methods.

Purposely omitted are data readily found in pharmacopœia, or generally available in handbooks. While there is as yet no description of qualitative and quantitative biological test methods, the reviewer, (himself so interested in their development and application) confidently looks for their adoption and insertion in the next revision.

The information given is helpful, particularly because it is based on experience with the subject treated. While, naturally, not as comprehensixe in scope, it is comparable in general purpose to the book of methods of the Association of Official Agricultural Chemists (A. O. A. C.), which has become such a popular guide for analytical methods (tentative and official) in this country.

The federation deserves wholehearted recommendation for its efforts and best wishes for the success of its aim to perfect and unify the analytical methods for international use.

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